

10-25-04

6723,702

C. of C.

Please type a plus sign (+) inside this box →



PTO/SB/21 (05-03)

Approved for use through 04/30/2003. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

|   |   |  |  |
|---|---|--|--|
| <b>TRANSMITTAL FORM</b><br><br>(to be used for all correspondence after initial filing) |   | Application Number   | 09/780,752   |
|   |   | Filing Date  | February 9, 2001   |
|   |   | First Named Inventor   | CONRAD, KIRK P.  |
|   |   | Group Art Unit   | 1653   |
|   |   | Examiner Name  | LIU, SAMUEL W.   |
| Total Number of Pages in This Submission  |   | Attorney Docket Number   | CONN-001   |
| <b>ENCLOSURES (check all that apply)</b>  |   |  |  |
| <input type="checkbox"/> Fee Transmittal Form   | <input type="checkbox"/> Assignment Papers (for an Application)           | <input type="checkbox"/> After Allowance Communication to Group                            | <b>of Correction</b><br><br><input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences<br><br><input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)<br><br><input type="checkbox"/> Proprietary Information<br><br><input type="checkbox"/> Status Letter<br><br><input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):<br>1) Petition for Certificate of Correction (1 pg.)<br>2) Certificate of Correction (1 pg.)<br>3) Copy of Issue Fee as filed on 02/27/2004 (1 pg.)<br>4) Return Postcard<br>5) front page of issued patent (1 pg.) |
| <input type="checkbox"/> Fee Attached   | <input type="checkbox"/> Drawing(s)                                       | <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences        |  |
| <input type="checkbox"/> Amendment / Reply  | <input type="checkbox"/> Licensing-related Papers                         | <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) |  |
| <input type="checkbox"/> After Final  | <input type="checkbox"/> Petition   | <input type="checkbox"/> Proprietary Information   |  |
| <input type="checkbox"/> Affidavits/declaration(s)                                      | <input type="checkbox"/> Petition to Convert to a Provisional Application | <input type="checkbox"/> Status Letter   |  |
| <input type="checkbox"/> Extension of Time Request                                      | <input type="checkbox"/> Power of Attorney, Revocation                    |  |  |
| <input type="checkbox"/> Express Abandonment Request                                    | <input type="checkbox"/> Change of Correspondence Address                 |  |  |
| <input type="checkbox"/> Information Disclosure Statement                               | <input type="checkbox"/> Terminal Disclaimer                              |  |  |
| <input type="checkbox"/> Certified Copy of Priority Documents                           | <input type="checkbox"/> Request for Refund                               |  |  |
| <input type="checkbox"/> Response to Missing Parts/Incomplete Application               | <input type="checkbox"/> CD, Number of CD(s)                              |  |  |
| <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53            | Remarks   |  |  |
| <b>SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT</b>                                       |   |  |  |
| Signing Attorney/Agent (Reg. No.)   | PAULA A. BORDEN, 42,344<br>BOZICEVIC, FIELD & FRANCIS, LLP                |  |  |
| Signature   |   |  |  |
| Date  | October 21, 2004  |  |  |

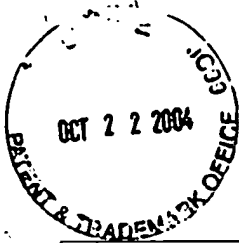
EXPRESS MAIL LABEL NO. EV519865930US

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

OCT 27 NOV 2004

17 NOV 2004



EXPRESS MAIL LABEL NO. **EV519865930US**

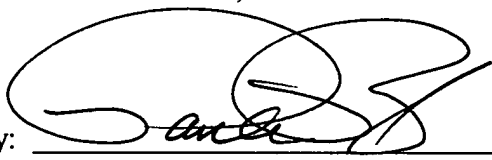
|   |                      |   |
|---|----------------------|---|
| <b>PETITION FOR CERTIFICATE OF CORRECTION</b><br><br>Address to:<br>Mail Stop DAC<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, VA 22313-1450 | Attorney Docket      | CONN-001  |
|   | First Named Inventor | CONRAD, KIRK P.   |
|   | Patent Number        | 6,723,702   |
|   | Issue Date           | April 20, 2004  |
|   | Application Number   | 09/780,752  |
|   | Filing Date          | February 9, 2001  |
|   | Title:               | <i>"USE OF RELAXIN TO TREAT DISEASES RELATED TO VASOCONSTRICTION"</i> |

Sir:

Transmitted herewith for filing is a Certificate of Correction for the above-identified patent. **Please delete "Ras Medical, Inc." and substitute therefore "BAS Medical, Inc" as indicated on the Issue Fee Transmittal mailed on February 27, 2004.** Enclosed is a copy of the Issue Fee Transmittal. Also enclosed is a copy of the front page of the issued patent showing the incorrect assignee name.

It is believed that no fee is due since the error was made by the Patent and Trademark Office. However, the Commissioner is hereby authorized to charge any fees under 37 C.F.R. § 1.20, which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815 order number CONN-001.

Respectfully submitted,  
BOZICEVIC, FIELD & FRANCIS LLP

By:   
Paula A. Borden  
Registration No. 42,344

BOZICEVIC, FIELD & FRANCIS LLP  
1900 University Avenue, Suite 200  
East Palo Alto, California 94303  
Telephone: (650) 327-3400  
Fax: (650) 327-3231

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.  
(Also form PTO-1050)

## UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

PATENT NO : 6,723,702  
DATED : April 20, 2004  
INVENTOR(S) : CONRAD, KIRK P., et al.

It is certified that error appears in the above-identified patent and that said Letters Patent  
is hereby corrected as shown below:

Please delete "Ras Medical, Inc." and substitute therefore "BAS Medical, Inc."

**MAILING ADDRESS OF SENDER:**

BOZICEVIC, FIELD & FRANCIS LLP  
1900 University Avenue, Suite 200  
East Palo Alto, California 94303

**PATENT NO. 6,723,702**

No. of additional copies



Burden Hour Statement: This form is estimated to take 1.0 hour to complete. Time will vary depending upon the needs of the individual case. Any comment on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

7 NOV 2004

## PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail

Mail Stop ISSUE FEE  
 Commissioner for Patents  
 P.O. Box 1450  
 Alexandria, Virginia 22313-1450  
 or Fax (703) 746-4000

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 4 should be completed where appropriate. Further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

24353 7590 12/03/2003

BOZICEVIC, FIELD & FRANCIS LLP  
 200 MIDDLEFIELD RD  
 SUITE 200  
 MENLO PARK, CA 94025

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

## Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO, on the date indicated below.

|                  |                    |
|------------------|--------------------|
| Express Mail No. | (Depositor's name) |
| EV33399070 US    | (Signature)        |
|                  | (Date)             |

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/780,752      | 02/09/2001  | Kirk P. Conrad       | CONN-001            | 6620             |

TITLE OF INVENTION: USE OF RELAXIN TREAT DISEASES RELATED TO VASOCONSTRICTION

| APPLN. TYPE    | SMALL ENTITY | ISSUE FEE | PUBLICATION FEE | TOTAL FEE(S) DUE | DATE DUE   |
|----------------|--------------|-----------|-----------------|------------------|------------|
| nonprovisional | NO           | \$1330    | \$300           | \$1630           | 03/03/2004 |

| EXAMINER      | ART UNIT | CLASS-SUBCLASS |
|---------------|----------|----------------|
| LIU, SAMUEL W | 1653     | 514-012000     |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Paula A. Borden  
 2 Bozicevic, Field &  
 3 Francis, LLP

## 3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY AND STATE OR COUNTRY)

1) BAS Medical, Inc., San Mateo, CA; 2) The University of Medicine and Dentistry of New Jersey - Robert Wood Johnson Medical School, New Brunswick, New Jersey;  
 3) The University of Pittsburgh - Of the Commonwealth System of Higher Education, Pittsburgh,  
 Please check the appropriate assignee category or categories (will not be printed on the patent); ☐ individual ☒ corporation or other private group entity ☐ government

## 4a. The following fee(s) are enclosed:

- ☒ Issue Fee  
☒ Publication Fee  
☒ Advance Order - # of Copies 10

## 4b. Payment of Fee(s):

- ☐ A check in the amount of the fee(s) is enclosed.  
☐ Payment by credit card. Form PTO-2038 is attached.  
☒ The Director is hereby authorized by charge the required fee(s), or credit any overpayment, to Deposit Account Number 50-0815 (enclose an extra copy of this form).

Director for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.

(Authorized Signature) \_\_\_\_\_ (Date)

Paula A. Borden (Reg. No. 42,344) 02/27/2004

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant, a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMIT THIS FORM WITH FEE(S)

NOV 2004



US006723702B2

(12) **United States Patent**  
**Conrad et al.**

(10) **Patent No.:** **US 6,723,702 B2**  
 (45) **Date of Patent:** **Apr. 20, 2004**

(54) **USE OF RELAXIN TREAT DISEASES  
 RELATED TO VASOCONSTRICTION**

(75) **Inventors:** Kirk P. Conrad, Cranberry Township, PA (US); Martyn Lewis, Menlo Park, CA (US); Elaine N. Unemori, Oakland, CA (US); Xinfan Huang, Menlo Park, CA (US); Carol A. Tozzi, Jackson, NJ (US)

(73) **Assignees:** RAS Medical, Inc., San Mateo, CA (US); The University of Medicine and Dentistry of New Jersey - Robert Wood Johnson Medical School, New Brunswick, NJ (US); The University of Pittsburgh - of the Commonwealth System of Higher Education, Pittsburgh, PA (US)

(\*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) **Appl. No.:** 09/780,752

(22) **Filed:** Feb. 9, 2001

(65) **Prior Publication Data**

US 2002/0019349 A1 Feb. 14, 2002

**Related U.S. Application Data**

(60) Provisional application No. 60/181,408, filed on Feb. 9, 2000, provisional application No. 60/200,284, filed on Apr. 28, 2000, and provisional application No. 60/242,216, filed on Oct. 20, 2000.

(51) **Int. Cl.<sup>7</sup>** ..... A61K 38/00; C07K 14/64

(52) **U.S. Cl.** ..... 514/12; 514/2; 530/303; 424/198.1; 604/19

(58) **Field of Search** ..... 514/2, 12; 530/303; 424/198.1; 604/19

(56) **References Cited**

**U.S. PATENT DOCUMENTS**

4,624,804 A 11/1986 Voelter et al.  
 5,166,191 A 11/1992 Cronin et al.  
 5,451,572 A \* 9/1995 Cipolla et al. .... 514/21  
 5,952,296 A \* 9/1999 Bigazzi ..... 514/3  
 6,211,147 B1 \* 4/2001 Unemori ..... 514/2

**FOREIGN PATENT DOCUMENTS**

WO WO 95/07711 3/1995

**OTHER PUBLICATIONS**

Danielson, L. A. et al. (1999) Relaxin is a potent renal vasodilator in conscious rats. *J Clin Invest.* vol. 103, pp. 525-533.\*

Danielson L. A. et al. (Sep. 1998) *J. Am. Society of Nephrology*, vol. 9, p. 336A, Abstract No. A1707.\*

Ahokas, R. A. et al. (1989) Lack of evidence of a vasodepressor role for relaxin in spontaneously hypertensive and normotensive pregnant rats. *Am. J. Obstet. Gynecol.* vol. 161, pp. 618-622.\*

Charney et al. (1993) "The role of the coronary collateral circulation in limiting myocardial ischemia and infarct size." *Am. Heart J.*, vol. 126:937-945.

Harada et al. (1994) "Basic Fibroblast Growth Factor Improves Myocardial Function in Chronically Ischemic Porcine Hearts." *J. Clin. Invest.*, vol. 94:623-630.

Henry (1999) "Therapeutic Angiogenesis" *BMJ*, vol. 318:1536-9.

Lopez et al. (1998) "VEGF administration in chronic myocardial ischemia in pigs." *Cardiovascular Research*, vol. 40:272-281.

Losordo et al. (1998) "Gene Therapy for Myocardial Angiogenesis." *Circulation*, vol. 98:2800-2804.

Patel et al. (1999) "Safety of Direct Myocardial Administration of an Adenovirus Vector Encoding Vascular Endothelial Growth Factor 121." *Human Gene Therapy*, vol. 10:1331-1348.

Unger et al. (1994) "Basic fibroblast growth factor enhances myocardial collateral flow in a canine model." *Am. J. Physiol.*, vol. 266:H1588-1595.

Yang et al. (1998) "Substantially Attenuated Hemodynamic Responses to *Escherichia coli*-Derived Vascular Endothelial Growth Factor Given by Intravenous Infusion Compared with Bolus Injection." *The Journal of Pharmacology and Experimental Therapeutics*, vol. 284(1):103-110.

\* cited by examiner

**Primary Examiner**—Karen Cochrane Carlson

**Assistant Examiner**—Samuel W Liu

(74) **Attorney, Agent, or Firm**—Paula A. Borden; Bozicevic, Field & Francis, LLP

(57) **ABSTRACT**

The invention related to methods of treating disease related to vasoconstriction that is a major factor in hypertensive vascular diseases and vasodilation, generally comprising administering to an individual an effective amount of a pharmaceutically active relaxin. Relaxin functions to increase both vasodilation and angiogenesis in males as well as females, and is useful in treating a wide variety of diseases relating to vasoconstriction.

**17 Claims, 15 Drawing Sheets**

U.S. Pat. 6,723,702 B2